

October 27, 2008

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Transmitted via www.regulations.gov

Re: Docket No. FDA-2008-N-0389

To whom it may concern:

The Food and Drug Administration (FDA) has requested comments relevant to the implementation of Sec. 912 of the Food and Drug Administration Amendments Act of 2007 (FDAAA). Among other things, Sec. 912 generally prohibits, with certain exceptions, the introduction or delivery for introduction into interstate commerce of any food to which a drug or biologic has been added. The Biotechnology Industry Organization (BIO) writes to provide information regarding an important area of health research and development that should not be affected by Sec. 912 of the FDAAA.

Background

BIO is the world's largest biotechnology organization, providing advocacy, business development and communications services for more than 1,200 members worldwide. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology technologies. Corporate members range from entrepreneurial companies developing their first product to Fortune 100 multinationals. We also represent state and regional biotechnology-derived associations, service providers to the industry and academic centers.

Several BIO members are developing pharmaceuticals and other products in plants that have been genetically engineered to produce therapeutic substances. Producing pharmaceutical substances from plants is a new application of biotechnology, and medicines produced from these plants represent one of the brightest new hopes in medicine. While great strides have been made through biotechnology in the search for new treatments and cures for diseases, research and development of biotechnology-derived drugs may be cut short due to capacity and cost issues. For example, hundreds of so-called "orphan diseases," devastating diseases affecting only a small number of individuals, may never benefit from drug research because of the small potential for return on investment. Plants may offer a cost-effective, sustainable, and faster source of medicines for patients, and provide access to new treatments which would otherwise be out of reach.

In the past few years, progress in the plant-made pharmaceutical (PMP) industry has advanced significantly – from the first regulatory approval of a plant-made animal vaccine, to successful clinical trial results in developing countries, to identifying the potential of producing insulin from



biotechnology-derived safflower. Several companies have shown the effectiveness of PMPs in addressing the medical needs of large and growing patient populations.

Regulation of PMP-producing Plants

The field research and production of plants producing PMPs is closely overseen by the United States Department of Agriculture's Animal and Plant Health Inspection Service (APHIS). All growing of PMP-producing plants is conducted either indoors, in greenhouses, or if conducted outdoors, under strict APHIS permits designed to protect both human health and the environment. *See* 7 C.F.R. Part 340. PMP-producing plants are grown and processed separately from crops intended for food and feed use in a completely closed loop system. APHIS, "Guidance for APHIS Permits for Field Testing or Movement of Organisms intended for Pharmaceutical or Industrial Use," available at http://www.aphis.usda.gov/brs/pdf/Pharma_Guidance.pdf.

APHIS must approve a PMP developer's standard operating procedures (SOPs) to prevent commingling with food or feed crops, the environment, humans and non-target organisms. These SOPs are based on scientific risk assessments that evaluate the potential for and impact of exposure, and are modeled after Hazard Analysis and Critical Control Point (HACCP) principles. As FDA is well aware, HACCP is a system currently in use in the food industry and identifies hazards and critical control points, and then establishes procedures for maintaining those points. The PMP industry has named its risk assessment Containment Analysis and Critical Control Point (CACCP).

These risk assessments developed for plant-made pharmaceuticals take into account the crop, the specific protein, the spatial setting or location of the intended production area and agronomic and crop handling practices. Confinement measures include both spatial isolation and temporal separation. Spatial confinement defines the distance between plots for plants producing pharmaceutical proteins and plants used for food and feed. Temporal boundaries define the time separating the flowering and pollination between plants producing pharmaceutical proteins and nearby plants of the same or related species.

Additionally, farm equipment that is used for plants producing PMPs cannot be used for any crops intended for food or feed use. The annual training of contract growers and all other individuals involved with the development and production of PMPs is an APHIS regulatory requirement. An APHIS-approved training program ensures personnel are prepared to successfully implement and comply with all permit conditions. Federal regulations are designed to prevent PMP-producing plants from crossing paths with crops used for food and feed production, making it highly unlikely for commingling to occur. APHIS inspects these plants at least six times during their growth and post-harvest, to ensure that all SOPs are followed. Importantly, at no time does the ownership of the PMP (seeds, plants and grains) change. The APHIS permit holder maintains ownership and control from breeding, through planting, harvesting, transport and processing.

Some PMPs are produced in plants from species that are also used for food or feed crops. However, as discussed above, at all times, PMPs are regulated under APHIS permit to ensure that the seed or grain does not enter the food chain or the environment, and sole ownership of the material is maintained. For some of these products, they will never be used as food, although they are produced in plants from species that are also used for food crops. In instances where PMP crops are

intended for use as foods or dietary supplements and enter interstate commerce, they should be treated the same under the FDAAA as foods or dietary supplements derived from other sources.

As recently as earlier this month, APHIS has affirmed its long-standing position that, under its current strict regulation and oversight, the development of PMPs in food crops poses no threat to the environment or public health: “APHIS concludes that the proposed permitting procedure and the use of stringent permit conditions *can continue to effectively minimize the risks* that may be associated with the environmental release of [PMPs]. APHIS will continue to impose permit conditions that take into account the issues related to the safety of proteins or other substances that these plants have been engineered to produce.” 73 Fed. Reg. 60008, 60020 (Oct. 9, 2008) (proposing revisions to regulations governing PMPs) (emphasis added).

There is no indication that it was the intent of Congress to include PMP production in the prohibitions set out in Sec. 912 of the FDAAA. Nothing in the statute prohibits PMP production in plant species that are also used for food or feed crops.

BIO appreciates the opportunity to provide the perspective of its members on this important issue. BIO welcomes the opportunity to provide additional information on its members working in this area as FDA moves forward with its implementation of Sec. 912 of the FDAAA.

Sincerely,

A handwritten signature in black ink that reads "Michael Wach". The signature is written in a cursive, flowing style.

Michael Wach
Managing Director, Science and Regulatory Affairs
Food and Agriculture Department
Biotechnology Industry Organization